Gpride®-M SR Tablets

(Glimepiride + Metformin HCl)

DESCRIPTION:
Gpride®-M SR a fixed dose combination (FDC) of glimepiride and metformin HCl contains glimepiride which is chemically 1-[[p-[2-(3-Ethyl-4-methyl-2-oxo-3-pyrroline-1-carboxamido) ethyl]phenyl]-sulphonyl]-3-(trans-4-methylcyclohexyl)urea and metformin HCl which is chemically 1,1-dimethyl biguanide hydrochloride

COMPOSITION:

Gpride®-M SR 1mg/500mg Tablets	Gpride®-M SR 2mg/500mg Tablets
Each bilayered tablet contains:	Each bilayered tablet contains:
Glimepiride USP.....1mg	Glimepiride USP.....2mg
Metformin HCl BP (as sustained release)...500mg	Metformin HCl BP (as sustained release)...500mg

CLINICAL PHARMACOLOGY:
Mechanism of Action:
Glimepiride: Glimepiride primarily lowers blood glucose by stimulating the release of insulin from pancreatic beta-cells. Sulfonylureas bind to the sulfonylurea receptor in the pancreatic beta-cell plasma membrane, leading to closure of the ATP-sensitive potassium channel, thereby stimulating the release of insulin
Metformin HCl: Metformin is an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization

INDICATIONS:
For Glimepiride and Metformin:
- As an adjunct to diet and exercise in type 2 diabetes mellitus patients
- In case that the monotherapy with glimepiride or metformin does not result inadequate glycemic control
- Replacement of combination therapy of glimepiride and metformin

DOSAGE AND ADMINISTRATION:
Dosage: In principle, the dosage is governed by the desired blood glucose level. The dosage of Gpride®-M SR must be the lowest which is sufficient to achieve the desired metabolic control. Mistakes, e.g. forgetting to take a dose, must never be corrected by subsequently taking a larger dose. The highest recommended dose per day should be 8mg of glimepiride and 2000mg of metformin. Daily doses of glimepiride of more than 6mg are more effective only in a minority of patients. In order to avoid hypoglycemia the starting dose of Gpride®-M SR should not exceed the daily doses of glimepiride or metformin already being taken. When switching from combination therapy of glimepiride plus metformin as separate tablets, Gpride®-M SR should be administered on the basis of dosage currently being taken

Administration: Gpride®-M SR should be administered once per day during breakfast or the first main meal. Due to the sustained release formulation, Gpride®-M SR must be swallowed whole and not crushed or chewed

Titration: The daily dose should be titrated in increments of 1 tablet only, corresponding to the lowest strength (in case various strengths are available)

Duration of treatment: Treatment with Gpride®-M SR is normally a long-term therapy

OR
As directed by the physician

PAEDIATRIC USE: Data are insufficient to recommend paediatric use of Gpride®-M SR

ADVERSE REACTIONS:
Please tell your physician or pharmacist if you experience any adverse effect with the use of Gpride®-M SR

For Glimepiride and Metformin:
The use of a combination of both compounds, either as a free combination or as a fixed combination, is associated with the same safety characteristics as the use of each compound separately

For Glimepiride:
Metabolism and nutrition disorders: As a result of the blood glucose lowering action of glimepiride, hypoglycemia may occur, which may also be prolonged. Possible symptoms of hypoglycemia include headache, ravenous hunger, nausea, vomiting, lassitude, sleepiness, disordered sleep, restlessness, aggressiveness, impaired concentration, impaired alertness and reactions, depression, confusion, speech disorders, aphasia, visual disorders, tremor, pareses, sensory disturbances, dizziness, helplessness, loss of self-control, delirium, cerebral convulsions, somnolence and loss of consciousness up to and including coma, shallow respiration and bradycardia. In addition, signs of adrenergic counter-regulation may be present such as sweating, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris, and cardiac arrhythmias
Eye disorders: Especially at the start of treatment, there may be temporary visual impairment due to the change in blood glucose levels. The cause is a temporary alteration in the turgidity and hence the refractive index of the lens, this being dependent on blood glucose level
Gastrointestinal disorders: Occasionally, gastrointestinal symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhoea may occur. In isolated cases, there may be hepatitis, elevation of liver enzyme levels and/or cholestasis and jaundice, which may progress to life threatening liver failure but can regress after withdrawal of glimepiride
Blood and lymphatic system disorders: Changes in the blood picture may occur: Rarely, thrombopenia and, in isolated cases, leucopenia, haemolytic anaemia, erythrocytopenia, granulocytopenia, agranulocytosis or pancytopenia may develop
General disorders: Occasionally, allergic or pseudoallergic reactions may occur, e.g. in the form of itching, urticaria or rashes. Such mild reactions may develop into serious reactions with dyspnoea and a fall in blood pressure, sometimes progressing to shock. In the event of urticaria a physician must therefore be notified immediately. In isolated cases, a decrease in serum sodium concentration and allergic vasculitis or hypersensitivity of the skin to light may occur

For Metformin:
Gastrointestinal symptoms: Such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite (>10%) are very common: these occur most frequently during initiation of therapy and resolve spontaneously in most cases. To prevent these gastrointestinal symptoms, it is recommended that metformin be taken in 2 or 3 daily doses during or after meals. A slow increase of the dose may also improve gastrointestinal tolerability
Skin Disorders: Mild erythema has been reported in some hypersensitive individuals. The incidence of such effects is regarded as very rare (<0.01%)
Others:
- A decrease of vitamin B12 absorption with decrease of serum levels has been observed in patients treated long-term with metformin and appears generally to be without clinical significance (<0.01%)
- Metallic taste (3%) is common

Lactic acidosis (0.03 cases/1000 patient -years) is very rare

CONTRAINDICATIONS:
For Glimepiride:
- In patients hypersensitive to glimepiride, other sulfonylureas, other sulfonamides, or any of the excipients of Gpride®-M SR
- No experience has been gained concerning the use of glimepiride in patients with severe impairment of liver function and in dialysis patients. In patients with severe impairment of hepatic function, change over to insulin is indicated, not least to achieve optimal metabolic control

For Metformin:
- Hypersensitivity to metformin or any of the excipients
- Diabetic ketoacidosis, diabetic pre-coma
- Renal failure or renal dysfunction (e.g., serum creatinine levels >135 micromol/L in males and > 110micromol/L in females)
- Acute conditions with the potential to alter renal function such as dehydration, severe infection, shock, intravascular administration of iodinated contrast agents, acute or chronic disease which may cause tissue hypoxia such as cardiac or respiratory failure, recent myocardial infarction, shock, hepatic insufficiency, lactation

PRECAUTIONS:
For Glimepiride:
In the initial weeks of treatment, the risk of hypoglycemia may be increased and necessitates especially careful monitoring

For Metformin:
Renal function: As metformin is excreted by the kidney, serum creatinine levels should be determined before initiating treatment and regularly thereafter:

- At least annually in patients with normal renal function
- At least two to four times a year in patients with serum creatinine levels at the limit of normal and in elderly subjects. Special caution should be exercised in situations where renal function may become impaired, for example when initiating antihypertensive therapy or diuretic therapy and when starting therapy with an NSAID

Administration of iodinated contrast agent: As the intravascular administration of iodinated contrast materials in radiologic studies can lead to renal failure, metformin should be discontinued prior to, or at the time of the test and not reinstituted until 8 hours afterwards, and only after renal function has been re-evaluated and found to be normal
Surgery: Metformin HCl should be discontinued 48 hours before elective surgery with general anaesthesia and should not be usually resumed earlier than 48 hours afterwards
Other Precautions:
- All patients should continue their diet with a regular distribution of carbohydrate intake during the day. Overweight patients should continue their energy-restricted diet
- The usual laboratory tests for diabetes monitoring should be performed regularly
- Metformin alone never causes hypoglycemia, although caution is advised when it is used in combination with insulin or sulfonylureas

PREGNANCY:
For Glimepiride: Glimepiride must not be taken during pregnancy. Otherwise there is risk of harm to the child. The patient must change over to insulin during pregnancy. Patients planning a pregnancy must inform their physician. It is recommended that such patients change over to insulin
For Metformin: To date, no relevant epidemiological data are available. Animal studies do not indicate harmful effects with respect to pregnancy, embryonal or fetal development, parturition or postnatal development

LACTATION:
For Glimepiride: To prevent possible ingestion with the breast milk and possible harm to the child, glimepiride must not be taken by breast-feeding women. If necessary the patient must change over to insulin, or must stop breast feeding
For Metformin: Metformin is excreted into milk in lactating rats. Similar data is not available in humans and a decision should be made whether to discontinue nursing or to discontinue metformin, taking into account the importance of the compound to the mother

WARNINGS:
For Glimepiride: In exceptional stress situations (e.g. trauma, surgery, febrile infections) blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary to maintain good metabolic control
For Metformin:
Lactic acidosis: Lactic acidosis is a rare, but serious (high mortality in the absence of prompt treatment), metabolic complication that can occur due to metformin accumulation. Reported cases of lactic acidosis in patients on metformin have occurred primarily in diabetic patients with significant renal failure. The incidence of lactic acidosis can and should be reduced by assessing also other associated risk factors such as poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake, hepatic insufficiency and any condition associated with hypoxia

DRUG INTERACTIONS:
For Glimepiride: Glimepiride is metabolized by cytochrome P450 2C9 (CYP2C9). This should be taken into account when glimepiride is co-administered with inducers (e.g. rifampicin) or inhibitors (e.g. fluconazole) of CYP 2C9. Potentiation of the blood glucose lowering effect and thus, in some instances hypoglycemia may occur when one of the following drugs is taken, for example insulin and other, oral antidiabetics; ACE inhibitors; anabolic steroids and male sex hormones; chloramphenicol; coumarin derivatives; cyclophosphamide; disopyramide; fenfluramine; fenyramidol; fibrates;fluoxetine; guanethidine; ifosfamide; MAO inhibitors; miconazole; fluconazole; para-aminosalicylic acid; pentoxifylline (high dose parenteral); phenylbutazone;azapropazone; oxyphenbutazone; probenecid; quinolones; salicylates; sulfinpyrazone;clarithromycin; sulfonamide antibiotics; tetracyclines; tritoqualine; trofosfamide.Weakening of the blood glucose lowering effect and, thus raised blood glucose levels may occur when one of the following drugs is taken, for example: acetazolamide;barbiturates; corticosteroids; diazoxide; diuretics; epinephrine (adrenaline) and other sympathomimetic agents; glucagon; laxatives (after protracted use); nicotinic acid (in high doses); oestrogens and progestogens; phenothiazines; phenytoin; rifampicin; thyroid hormones. H2 receptor antagonists, beta-blockers, clonidine and reserpine may lead to either potentiation or weakening of the blood glucose lowering effect. Under the influence of sympatholytic drugs such as beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation to hypoglycemia may be reduced or absent. Both acute and chronic alcohol intake may potentiate or weaken the blood glucose acidosis. Metformin should be discontinued prior to, or at the time of the test and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal
Associations Requiring Precautions for Use: Glucocorticoids (systemic and local routes), beta-2-agonists, and diuretics have intrinsic hyperglycaemic activity. Inform the patient and perform more frequent blood glucose monitoring, especially at the beginning of treatment. If necessary, adjust the dosage of the antidiabetic drug during therapy with the other drug and upon its discontinuation. ACE inhibitors may decrease the blood glucose levels. If necessary, adjust the dosage of the antidiabetic drug during therapy with the other drug and upon its discontinuation

OVERDOSAGE:
For Glimepiride:
Signs and Symptoms: Acute over-dosage as well as long-term treatment with too high a dose of glimepiride may lead to severe life threatening hypoglycemia
Management: As soon as an overdose of glimepiride has been discovered, a physician must be notified without delay. Careful monitoring is essential until the physician is confident that the patient is out of danger. It must be remembered that hypoglycemia may recur after initial recovery. Admission to hospital may sometimes be necessary - even as a precautionary measure. Patients who have ingested life threatening amounts of glimepiride required detoxification (e.g. by gastric lavage and medicinal charcoal)
For Metformin:
Hypoglycemia has not been seen with metformin doses of up to 85g, although lactic acidosis has occurred in such circumstances. High overdose or concomitant risks of metformin may lead to lactic acidosis. Lactic acidosis is a medical emergency and must be treated in hospital. The most effective method to remove lactate and metformin is haemodialysis

STABILITY:
See expiry on the pack

PRESENTATION:
- Gpride®-M SR 1mg/500mg tablets in pack of 30's
- Gpride®-M SR 2mg/500mg tablets in pack of 30's

INSTRUCTIONS:
To be swallowed whole with water
Keep out of reach of children
Avoid exposure to heat, light and humidity
Store between 15 to 30ºC
Improper storage may deteriorate the medicine

جی پرائیڈ-ایم ایس آر ٹیبلٹ
(گلی میپیرائیڈ + میٹ فورمن ہائیڈروکلورائیڈ)
خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں
ثابت ٹیبلٹ چبائے بغیر پانی سے نگل لیں
بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ
کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

Manufactured by:
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220 mm

71 mm